I. THE CLAIMS ARE PATENTABLE OVER THE REFERENCES CITED

The Examiner has rejected Claims 1, 13, and 15-16 under 35 U.S.C. 103(a) as allegedly being unpatentable over Essigmann *et al.* in view of Güler *et al.* The Applicant respectively submits the Examiner has failed to establish the elements of a *prima facie* case of obviousness under the law. *See, e.g., Northern Telecom Inc. v. Datapoint Corp.*, 15 U.S.P.Q. 2d 1321, 1323 (Fed. Cir. 1990);[1] *See also, In re Dembiczak*, 175 F.3d 994, 998 (Fed. Cir. 1999).

A. There Is No Motivation to Combine the References

A proper analysis, in view of 35 U.S.C. § 103, demands the references cited by the Examiner be considered as a whole and must suggest the desirability and thereby, the obviousness, of making the combination. *Hodash v. Block Drug Co.*, 786 F. 2d 1136, 1143, n.5, 229 U.S.P.Q. 182, 187, n.5 (Fed. Cir. 1986); *MPEP* § 2141.[2] Moreover, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." MPEP § 2141.01 (citing *In re Mills*, 916 F.2d 680, U.S.P.Q.2d 1430 (Fed. Cir. 1990).

The Examiner argues that:

> "[t]he motivation of using the *sqdI* and *sqdX* gene product is that the encoded enzymes can be used to produce SQDG of high yield and purity. An efficient production of SQDG is attractive because sulfolipids are possible anti-tumor and anti-HIV therapeutics." (Office Action Mailed 11/26/01, pp. 3 & 5).

---

[1] The Examiner is reminded that a prima facie case of obviousness requires citation to a combination of references which (A) suggests or motivates one of skill in the art to combine the elements to yield the claimed combination, (B) provides a reasonable expectation of success should the claimed combination be carried out, and (C) discloses the elements of the claimed embodiment. Failure to establish any one of these three requirements precludes a finding of a *prima facie* case of obviousness, and, without more, entitles Applicant to allowance of the claims in issue. *Northern Telecom Inc. v. Datapoint Corp.*, 15 U.S.P.Q. 2d 1321, 1323 (Fed. Cir. 1990).

[2] This proper analysis prevents the Examiner from using the instant Specification to reconstruct, in hindsight, the invention as claimed. The Federal Circuit articulated the policy behind this analysis:

> "To prevent the use of hindsight based on the invention to defeat patentability of the invention, this court requires the examiner to show a motivation to combine the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed."

In re Rouffet, 149 F.3d 1350, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998).

However, the Examiner has failed to indicate, *wherein the references cited*, there is such a suggestion of desirability to combine.

The Examiner asserts that Figure 1 of Essigmann *et al.* "outlines the pathway for SQDG synthesis." (Office Action Mailed 11/26/01, p. 5). However, as indicated in the Declaration of Dr. Christoph Benning (attached at Tab B):

> "the figure is completely silent on the use of a first and second recombinant (*i.e.* SQD1 and *sqdX* respectively) in a biochemical method to produce UDP-sulfoquinovose and SQDG. Figure 1 merely depicts *a "model* of the sugar-nucleotide pathway for sulfolipid biosynthesis" without providing direction as to the appropriate buffer conditions, sulfite, and recombinant enzymes required for a biochemical method to produce UDP-sulfoquinovose and SQDG as claimed by the present invention. There is also no suggestion of such an approach in the text of the Essigmann paper."

(Declaration of Christoph H. Benning, p.2).

Thus, Figure 1 (and the Essigmann paper itself) does not provide an outline for the pathway for SQDG biosynthesis utililzed by the embodiments of present invention as claimed. In fact, as Dr. Benning explained, Essigmann *et al.* merely:

> "describes experiments conducted to determine the structure of the active site of the SQD1 enzyme protein. The Essigmann paper is completely silent on how the enzyme protein works, whether the enzyme must be an active (*i.e.* functioning) protein, how one would express (*i.e.* recombinantly) and isolate such an active protein, or how one would assay its activity. Unlike the present invention, the Essigmann paper does not disclose all of the four *critical* elements of the enzymatic biosynthesis of UDP-sulfoquinovose: active SQD1 enzyme, UDP-glucose, sulfite, and the appropriate buffer conditions."

(Declaration of Christoph H. Benning, pp. 1-2).

Although Güler *et al.* teaches the use of a peptide encoded by the *sqdX* gene to produce SQDG, the reference neither teaches, nor suggests, using the peptides of the claimed embodiment and various sulfur groups (*i.e.* donors) in combination to produce SQDG. Therefore, the cited prior art does not suggest the desirability of making the combination of elements set forth in the claims at issue in the present case. Thus, the Examiner cannot point to a basis for combining the references.

Finally, Applicants respectfully remind the Examiner that the requirement that the Examiner make a showing of a suggestion, teaching or motivation to combine the prior art references is "an essential evidentiary component of an obviousness holding." *C.R. Bard, Inc.*

v. M3 Sys. Inc., 157 F.3d 1340, 1352 (Fed. Cir. 1998). There are three sources for this evidentiary component: the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. *Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Cir. 1996). The suggestion most often comes from the teachings of the pertinent references. *In re Rouffet*, 149 F.3d 1350, 1359 (Fed. Cir. 1998). Nonetheless, regardless of the source of the requisite evidence, the Examiner's showing "must be clear and particular, and broad conclusory statements about the teaching of multiple references, standing alone, are not 'evidence'." *In re Dembiczak*, 175 F.3d 994, 1000 (Fed. Cir. 1999).

Importantly, since an Examiner is not one skilled in the art (under the law), the Examiner's opinion on what one skilled in the art might believe does not count. *In re Rijckaert*, 9 F.3d 1531, 28 U.S.P.Q.2d 1955, 1956 (Fed. Cir. 1993) (stating that "the examiner's assumptions do not constitute the disclosure of the prior art."). Of course, if the Examiner has knowledge of relevant facts which are used to make the rejection, the Examiner is free to use those facts - but only if submitted in the form of an affidavit. *See* 37 C.F.R. § 1.107(b). In the present case, the Examiner has submitted no such affidavit.

Indeed, the Examiner has provided only the Examiner's opinion and conclusory statements - this is not the requisite "evidence" needed to support the combination. The Examiner simply asserts - without a basis - that based on the disclosure of Figure 1 in Essigmann *et al.*, coupled with the purported desirable properties of sulfolipids and advantages of making SQDG enzymatically rather than chemically, the present invention is rendered obvious under 35 U.S.C. § 103. The above-cited case law shows that this is not adequate evidence and the Examiner has not satisfied the requirements for combining the art.

B. The References Do Not Disclose a Reasonable Expectation of Success

A proper analysis under 35 U.S.C. § 103 requires that a combination of references must provide a reasonable expectation of success should the claimed combination be carried out. *MPEP* § 2143.02. Moreover, "both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck*, 20

U.S.P.Q.2d 1438, 1442, 947 F.2d 488 (Fed. Cir. 1991). The Examiner has failed to indicate, *wherein the references cited*, there is any such disclosure. The Examiner argues that:

> "One of ordinary skill in the art would have a reasonable expectation of success since Essigmann *et al.* outlines the pathway for SQDG production and the two references teach which enzyme is necessary for the pathway. Also, production of compounds using recombinant enzymes in lieu of chemical synthesis is routinely performed." (Office Action Mailed 11/26/01, pp. 5-6).

However, as noted above, Essigmann *et al.* (and particularly Figure 1) does not "provide direction as to the appropriate buffer conditions, sulfite, and recombinant enzymes required for a biochemical method to produce UDP-sulfoquinovose and SQDG as claimed by the present invention." (Declaration of Christoph H. Benning, p. 2). Moreover, Essigmann *et al.* teaches that the identity of the sulfur donor involved in sulfolipid biosynthesis is *unknown* (*see* Essigmann *et al.*, p. 36, Col. 2, 1st paragraph). Indeed, Essigmann *et al.* makes a statement on page 38 in regard to the sulfur donor which should - by itself - demonstrate the fatal deficiencies of the reference:

> ". . . a functional assay for SQD1 activity is **not yet possible due to the unknown identity of the sulfur donor** . . ."

A patent examiner is not free to speculate on a point, where the reference itself says it "not yet possible." Thus, without the appropriate sulfur donor and buffer conditions, there is no "reasonable expectation of success" since at least two of the critical elements of the present invention are missing. Güler *et al.* provides no guidance with respect to the critical elements lacking in the Essigmann *et al.* Whether or not the "production of compounds with recombinant enzymes is performed routinely" is of no moment (*i.e.* the focus here is on the biochemical synthesis of UDP-SQ and SQDG as contemplated by the present invention). Essigmann *et al.* and Güler *et al.* are similarly silent with respect to whether one skilled in the art would have a reasonable expectation of success should the claimed combination be carried out.

C. Even if Combined (Improperly), The References Do Not Teach All of The Elements

The Examiner asserts that Essigmann et al. "teach that sulfite can be used as the sulfur donor." (Office Action Mailed 11/26/01, p. 2). However, as noted is the attached declaration by Dr. Christoph Benning:

> "the discussion of a 'sulfur donor' is made within the context of a chemical synthesis scheme. The papers cited as references 43 and 44 in support of the discussion of sulfite all refer to *chemical synthesis* reactions, not *enzymatic biosynthesis* methods.[3] The Essigmann paper only suggests a model of how a plant may make sulfite. The paper does not disclose that sulfite is 'the' sulfur donor in an enzymatic biosynthesis method to produce UDP-sulfoquinovose by using SQD1, UDP-glucose, sulfite, and the appropriate buffer conditions."

(Declaration of Christoph H. Benning, p.2, attached at Tab B)(emphasis added).

In fact, Essigmann *et al.* teaches that the identity of the sulfur donor involved in sulfolipid *biosynthesis* is *unknown* (*see* Essigmann *et al.*, p. 36, Col. 2, 1st paragraph). Simply put, the Examiner has misunderstood the cited reference.

The Examiner argues that Figure 1 of Essigmann *et al.* "teaches a pathway for the synthesis of SQDG," and that SQD1 catalyzes formation of UDP-SQ from UDP and a sulfur donor. (Office Action Mailed 11/26/01, p. 6). However, as noted above, "Figure 1 merely depicts one *'model* of the sugar-nucleotide pathway for sulfolipid biosynthesis' without providing direction" (*i.e.* critical elements of the invention are missing).

Although Güler *et al.* teaches the use of a peptide encoded by the *sqdX* gene to produce SQDG, Dr. Benning's declaration clearly states that:

> "[t]he reference is completely silent on the use of a first and second recombinant peptide (*i.e.* SQD1 and *sqdX* respectively) in a biochemical method to produce UDP-sulfoquinovose and convert it to SQDG. The reference neither discusses, nor suggests, the *critical* elements of the enzymatic biosynthesis of UDP-sulfoquinovose and its conversion to SQDG: active SQD1 enzyme, UDP-glucose, sulfite (as the sulfur donor), active sqdX (or AtSQDX-1) enzyme, diacylglycerol, and the appropriate buffer conditions."

(Declaration of Christoph H. Benning, p.2, attached at Tab B).

---

[3] Moreover, the paper cited as reference 41 only discusses sugar modifying enzymes in general and mentions UDP-4-keto-5,6-glucoseen (*i.e.* not UDP-SQ or SQDG). Reference 41 is also completely silent with respect to sulfite.

Thus, even if the Essigmann and Güler references were to be improperly combined, they still would not teach the production of UDP-sulfoquinovose, and its subsequent modification to SQDG, by a method using sulfite, uridine-5'-diphosphoglucose, and said recombinant peptides as claimed by the present invention.

The Examiner concludes that:

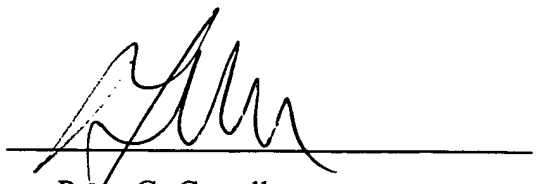
> "[s]ince the enzymes catalyzing the sequential steps are taught, one of ordinary skill in the art would have been motivated to carry out the reaction using the enzymes instead of chemically synthesizing SQDG to obtain higher yield and purity." (Office Action Mailed 11/26/01, p. 6).

However, "the deficiencies of the cited references cannot be remedied by the [Examiner's] general conclusions about what is 'basic knowledge' or 'common sense' to one of ordinary skill in the art." *In re Zurko*, 258 F.3d 1379, 1385 (Fed. Cir. 2001). The elements of the claimed embodiment is not taught as is required in a proper analysis under 35 U.S.C. § 103; *MPEP* § 2143.03. Therefore, the claims should be allowed.

The Examiner has failed to provide a reference or combination of references which reasonably suggests or teaches the limitations of the claims at issue. Therefore the rejection appears to be based on the Examiner's beliefs rather than the prior art. This is improper. Accordingly, the Claims 1, 13, 15 & 16, are not obvious and should be passed to allowance.

CONCLUSION

The Applicant believes that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that these grounds for rejection be withdrawn for the reasons set above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants' encourage the Examiner to call the undersigned collect at 617.252.3353.

Dated: March 11, 2002 Signed: 

Peter G. Carroll
Registration No. 32,837
MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105